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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,307	01/11/2001	Sam J. Milstein	1946/1A483-US8	8759

7590 11/03/2006

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,307	MILSTEIN ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6-22-06&7-10-06*. 1/27/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 13-16,22-26,31-36,50-53,59-62,68-73,87-90,96-99,105-110,112-127,131-137,139-150,152-163,165-176 and 178-195.

Continuation of Disposition of Claims: Claims rejected are 13-16,22-26,31-36,50-53,59-62,68-73,87-90,96-99,105-110,112-127,131-137,139-150,152-163,165-176 and 178-195.

DETAILED ACTION

Receipt of IDS dated 6-22-06 & 7-10-06 and response dated 7-19-06 is acknowledged. Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, 112-127, 131-137, 139-150, 152-163, 165-176 and 178-195 are pending in the instant application.

Response to Arguments

Applicant's arguments filed 7-19-06 have been fully considered but they are not persuasive.

The following rejection of record has been maintained:

1. Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, and 112-127, 131-137,139-150, 152-163, 165-176, and 178-195 stand rejected under the judicially created doctrine of obviousness-type double patenting over various claims of U.S. Patent Nos. 6,071,538; 5,714,167; 6,348,207 and 6,221,367.

2. Claims 13-37, 50-74 and 87-189 are directed to an invention not patentably distinct from claims 1-5 and 11-20 of commonly assigned US 6,071,538, claims 1-22 and 33-37 of U.S. Patent No. 6, 348,207 ('207) and claims 1-7 of U.S. 5,714,167 ('167).

3. Claims 13-37, 50-74 and 87-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over 6,017,538 (hereafter '538), 6,348,207 ('207) or 5,714,167 ('167).

4. Claims 13-37, 50-74 and 87-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of U.S. Patent No. 6,221,367. Although the conflicting claims are not identical, they are not patentably distinct from each other because the perturbant of the patented claims is a species the generic perturbants claimed in the instant invention.

RESPONSE: Applicants argue that while the rejections are traversed upon the finding of allowable subject matter, applicants will consider filing a terminal disclaimer. At this time, no allowable claims are present and hence the rejection has been maintained.

5. Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 are rejected under 35 U.S.C. 103(a) as being unpatentable over Makino et al (US Patent No. 4,746,675) in view of Morishita et al (US Patent No. 4,873,087).

Morishita teaches a preparation containing an absorption promoter and a medically active agent for promoting absorption through a gastrointestinal organ such as colon, rectum or through vagina. The absorption promoter substance of Morishita is an N-acyl amino acid or N-acyl peptide derivative, of formula I (col. 1, lines 5-10, col. 3, lines 13-15) and is obtained by the reaction of an acid (R-COOH) with an amino acid or peptide. The carboxylic acids and amino acids used for preparing N-acyl amino acids are described in col. 4 and 6 and include those described in the instant specification. Among the medically active agent, Morishita describes hormones, such as insulin, antibiotics etc (col. 5, lines 25-68). Morishita fails to specifically teach that the absorption promoter is non-covalently linked to the active agent or the molecular weight of the promoter. However, Morishita teaches the same components of the instant claims and accordingly the burden is shifted to applicants to show how the teachings of Morishita differ from the instant. Morishita does not specifically teach subcutaneous,

intranasal or sublingual delivery routes, instead teaches administration through rectum or vagina, which are lined by mucosal membranes.

Makino teaches external pharmaceutical composition for administering therapeutic agents via skin and mucosal membranes. The compositions of Makino comprise a pharmacologically active agent and a penetration enhancer, such as pyroglutamic acid derivatives (col. 4-8). The pyroglutamic acid derivatives shown by formula I (col. 4) of Makino read on the claimed acylated amino acid derivatives. Makino teaches a number of pharmaceutically active agents that can be administered using the above absorption enhancer (col. 10-12), which include those that are claimed in the instant application. Makino teaches that the penetration enhancers are capable of penetrating skin or mucosa and thus can enhance the absorption a wide range of (hydrophilic as well as hydrophobic) drugs; and also when administered by oral or injection route, the absorption enhancer prevents the drug from being degraded and maintain the effective blood levels over a long period of time (col. 3-4). The claimed routes of sublingual, intranasal involve mucosal administration. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ the pyroglutamic acid derivatives of Makino as absorption enhancers for a variety of pharmaceutical agents, administered by sublingual or intranasal or subcutaneous routes because Makino teaches that the compounds are extremely useful in delivering drugs orally, topically or mucosally without loosing the activity due to degradation or lack of transport through the mucosal or epidermal membranes. Similarly, it would have obvious for one of an ordinary skill in the art at the time of the

instant invention to administer the absorption enhancers of Morishita via mucosal routes (sublingual or intranasal) or subcutaneous injection because Makino suggests that the amino acid derivatives are effective in delivering a number of drugs administered by oral or injection or via skin or mucosal membrane, without loosing the activity of the drugs.

RESPONSE:

It is argued that examiner has not satisfied the burden to establish motivation to combine simply based on purported teaching of a penetration enhancer and oral or injection routes of administration, and Morishita teaching of composition using different compounds to enhance absorption through the colon, rectum or vagina. It is argued that Makino actually teaches away from injection as opposed to examiner's contention. Further, it is argued that the combined teachings of Makino and Morishita do not teach each and every limitation because the acylated amino acids of Makino are different from the claimed compounds and the Morishita teaches the compounds as intermediates in the preparation of compounds of formula I. Applicants' arguments with respect to the rejection of claims over Makino and Morishita have been considered but not found persuasive because instant claims recite a method "for the administration" and not "of administration". Hence the argument that Makino teaches away from the claimed invention is not persuasive. Besides, the claims do not recite any steps of administering and instead only recites providing a perturbant and active agent. Morishita admittedly teach different routes of administration. With respect to the acylated amino acids, Morishita teaches compounds of formula I where A is an amino acid residue. The moieties R-CO and A read on the instant acylated amino acids because R of Morishita

read on Ar moiety and CO-A is an acyl moiety. Accordingly, the claims are prima facie obvious over the above teachings.

The following is a new rejection

Double Patenting

1. Claims 13-16, 23-26, 32-36, 50-53, 59-62, 69-78, 87-90, 97-99, 106-110, 112-127, 131-137, 139-150, 152-163, 165-176 and 178-195 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 9-18, 22-30 and 35-38 of U.S. 6,221,367 ('367); 1 and 22 of U.S. Patent No. 6,916,489 ('489); and 32-46 of U.S. Patent No. 7,005,141 ('141); claims 17, 18, 33-45 of US Patent No. 6,461,643 and claims 25-29 of US 5,629,090.

Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the claims of '367, '020, '643, 489 and '141 recite a method of preparing or delivering a biological agent comprising the claimed acylated amino acids as perturbant and a biologically active agent, wherein the perturbant that reversibly transforms the active agent upon non-covalent binding with the active agent and together both the perturbant and the active agent form a supra molecular complex. The above patents claim various routes of administration that overlap with the instant claims. Further, instant claims do not recite the steps of administering the compositions by different and instead only claim a method "for administering" the composition comprising an active agent and the claimed perturbant. The above patented claims

specifically recite acylated amino acids and the claimed biological agents and therefore it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the composition of the above patents containing an active agent and a perturbant that reversibly transform the active agent for administering via intranasal or sublingual or subcutaneous routes because the above patents recite the same perturbants in transporting the active agents, irrespective of the mode of administration i.e., the changed or altered confirmation of the active agents renders the active agent to cross and penetrate cell membranes. Accordingly, one of an ordinary skill in the art would have expected to transport the active agents of using the perturbants across other mucosal membranes such as those of nasal tissues or the mouth cavity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Art Unit 1615

October 30, 2006

LAKSHMI S. CHANNAVAJJALA
PRIMARY EXAMINER